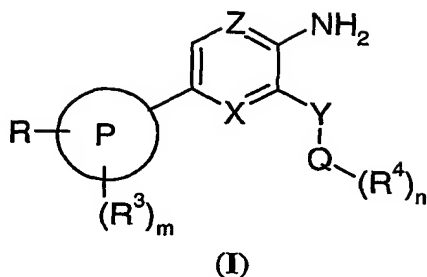


CLAIMS

1. A compound having the formula I



wherein:

Z is N;

Y is CONR⁵, NR⁵CO, SO₂NR⁵, NR⁵SO₂, CH₂NR⁵, NR⁵CONR⁵, CH₂CO, CO or CH₂O;

10 X is CH or N;

P is phenyl or a 5 or 6 membered heteroaromatic ring containing one or more heteroatoms selected from N, O or S and said phenyl ring or 5 or 6 membered heteroaromatic ring may optionally be fused with a 5 or 6 membered saturated, partially saturated or unsaturated ring containing atoms independently selected from C, N, O or S;

15 Q is C₁₋₆alkyl, C₂₋₆alkenyl or C₂₋₆alkynyl;

R is CHO, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C₀₋₆alkyl(SO₂)NR¹R², OC₀₋₆alkyl(SO₂)NR¹R², OC₁₋₆alkyl(SO)NR¹R², C₁₋₆alkyl(SO)NR¹R², C₀₋₆alkylNR¹(SO)R², OC₁₋₆alkylNR¹(SO)R², C₀₋₆alkylNR¹(SO₂)NR¹R², OC₁₋₆alkylNR¹(SO₂)R², C₀₋₆alkyl(SO₂)C₁₋₆alkylNR¹R², OC₀₋₆alkyl(SO₂)C₁₋₆alkylNR¹R², C₀₋₆alkyl(SO)C₁₋₆alkylNR¹R², OC₁₋₆alkyl(SO)C₁₋₆alkylNR¹R², C₀₋₆alkylSC₁₋₆alkylNR¹R², OC₁₋₆alkylSC₁₋₆alkylNR¹R², OC₁₋₆alkylOC₁₋₆alkyl, C₁₋₆alkylOC₁₋₆alkylNR¹R², OC₁₋₆alkylOC₁₋₆alkylNR¹R², C₀₋₆alkylCONR¹⁰R¹¹, OC₀₋₆alkylCONR¹R², OC₁₋₆alkylNR¹R², C₀₋₆alkylNR¹⁰(CO)R¹¹, OC₁₋₆alkylNR¹(CO)R², C₀₋₆alkylNR¹¹(CO)R¹⁰, C₀₋₆alkylCOR¹¹, OC₁₋₆alkylCOR¹, C₀₋₆alkylNR¹⁰R¹¹, C₀₋₆alkylO(CO)R¹¹, OC₁₋₆alkylO(CO)R¹, C₀₋₆alkylC(NR¹⁰)NR¹⁰R¹¹, C₀₋₆alkylC(NR¹¹)N(R¹⁰)₂, OC₀₋₆alkylC(NR¹)NR¹R², C₀₋₆alkylNR¹⁰(CO)OR¹¹, OC₁₋₆alkylNR¹(CO)OR²,

25

$C_{0-6}alkylNR^{11}(CO)OR^{10}$, $OC_{1-6}alkylCN$, NR^1OR^2 , $C_{0-6}alkyl(CO)OR^8$, $OC_{1-6}alkyl(CO)OR^1$, $NR^1(CO)NR^1R^2$, $NR^1(CO)(CO)R^2$, $NR^1(CO)(CO)NR^1R^2$, OR^{12} or SO_3R^1 ;

R^1 and R^2 are independently selected from hydrogen, $C_{1-6}alkyl$, $C_{2-6}alkenyl$, $C_{2-6}alkynyl$, $C_{0-6}alkylC_{3-6}cycloalkyl$, $C_{0-6}alkylheterocycloalkyl$, $C_{1-6}alkylNR^6R^7$,

5 $C_{0-6}alkylaryl$ and $C_{0-6}alkylheteroaryl$, wherein any $C_{1-6}alkyl$, $C_{2-6}alkenyl$, $C_{2-6}alkynyl$, $C_{0-6}alkylC_{3-6}cycloalkyl$, $C_{0-6}alkylheterocycloalkyl$, $C_{0-6}alkylaryl$, $C_{0-6}alkylheteroaryl$ may be substituted by one or more A;

R^1 and R^2 may together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring
10 may be optionally substituted by A;

R^3 is independently selected from halogen, nitro, CHO, $C_{0-6}alkylCN$, $OC_{1-6}alkylCN$, $C_{0-6}alkylOR^6$, $OC_{1-6}alkylOR^6$, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, $C_{0-6}alkylNR^6R^7$, $OC_{1-6}alkylNR^6R^7$, $OC_{1-6}alkylOC_{1-6}alkylNR^6R^7$, NR^6OR^7 , $C_{0-6}alkylCO_2R^6$, $OC_{1-6}alkylCO_2R^6$,

15 $C_{0-6}alkylCONR^6R^7$, $OC_{1-6}alkylCONR^6R^7$, $OC_{1-6}alkylNR^6(CO)R^7$, $C_{0-6}alkylNR^6(CO)R^7$, $O(CO)NR^6R^7$, $NR^6(CO)OR^7$, $NR^6(CO)NR^6R^7$, $O(CO)OR^6$, $O(CO)R^6$, $C_{0-6}alkylCOR^6$, $OC_{1-6}alkylCOR^6$, $NR^6(CO)(CO)R^6$, $NR^6(CO)(CO)NR^6R^7$, SR^6 , $C_{0-6}alkyl(SO_2)NR^6R^7$, $OC_{1-6}alkylNR^6(SO_2)R^7$, $OC_{0-6}alkyl(SO_2)NR^6R^7$, $C_{0-6}alkyl(SO)NR^6R^7$, $OC_{1-6}alkyl(SO)NR^6R^7$, SO_3R^6 , $C_{0-6}alkylNR^6(SO_2)NR^6R^7$, $C_{0-6}alkylNR^6(SO)R^7$,

20 $OC_{1-6}alkylNR^6(SO)R^7$, $OC_{0-6}alkylSO_2R^6$, $C_{0-6}alkylSO_2R^6$, $C_{0-6}alkylSOR^6$, $C_{1-6}alkyl$, $C_{2-6}alkenyl$, $C_{2-6}alkynyl$, $C_{0-6}alkylC_{3-6}cycloalkyl$, $C_{0-6}alkylaryl$ and $C_{0-6}alkylheteroaryl$, wherein any $C_{1-6}alkyl$, $C_{2-6}alkenyl$, $C_{2-6}alkynyl$, $C_{0-6}alkylC_{3-6}cycloalkyl$, $C_{0-6}alkylaryl$ and $C_{0-6}alkylheteroaryl$ may be optionally substituted by one or more A;

R^4 is independently selected from halogen, nitro, CHO, CN, $OC_{1-6}alkylCN$, OR^6 ,

25 $OC_{1-6}alkylOR^6$, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, NR^6R^7 , $OC_{1-6}alkylNR^6R^7$, NR^6OR^7 , CO_2R^6 , $OC_{1-6}alkylCO_2R^6$, $CONR^6R^7$, $OC_{1-6}alkylCONR^6R^7$, $OC_{1-6}alkylNR^6(CO)R^7$, $NR^6(CO)R^7$, $O(CO)NR^6R^7$, $NR^6(CO)OR^7$, $NR^6(CO)NR^6R^7$, $O(CO)OR^6$, $O(CO)R^6$, COR^6 , $OC_{1-6}alkylCOR^6$, $NR^6(CO)(CO)R^6$, $NR^6(CO)(CO)NR^6R^7$, SR^6 , $(SO_2)NR^6R^7$,

30 $OC_{1-6}alkylNR^6(SO_2)R^7$, $OC_{0-6}alkyl(SO_2)NR^6R^7$, $(SO)NR^6R^7$, $OC_{1-6}alkyl(SO)NR^6R^7$, SO_3R^6 , $NR^6(SO_2)NR^6R^7$, $NR^6(SO)R^7$, $OC_{1-6}alkylNR^6(SO)R^7$, $OC_{0-6}alkylSO_2R^6$, SO_2R^6 , SOR^6 , $C_{3-6}cycloalkyl$, phenyl, a 5 or 6 membered heteroaromatic ring containing one or

- more heteroatoms independently selected from N, O, or S, or a 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O, or S which heterocyclic group may be saturated or unsaturated, and said phenyl ring or 5 or 6 membered heteroaromatic ring or 5 or 6 membered heterocyclic ring may optionally be
- 5 fused with a 5 or 6 membered saturated, partially saturated or unsaturated ring containing atoms independently selected from C, N, O or S wherein any C₃₋₆cycloalkyl, phenyl, 5 or 6 membered heteroaromatic ring with one or two heteroatoms selected independently from N, O, or S or a 5 or 6 membered heterocyclic containing one or two heteroatoms selected independently from N, O, or S; may be optionally be substituted by one or more A;
- 10 m is 0, 1, 2, 3 or 4;
n is 0, 1, 2, 3 or 4;
R⁵ is hydrogen or C₁₋₆alkyl
R⁶ and R⁷ are independently selected from hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₀₋₆alkylC₃₋₆cycloalkyl, C₀₋₆alkylaryl, C₀₋₆alkylheteroaryl and C₁₋₆alkylNR⁸R⁹;
- 15 R⁶ and R⁷ may together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A and wherein a CH₂ group may optionally be replaced by a CO group;
R⁸ and R⁹ are independently selected from hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₀₋₆alkylC₃₋₆cycloalkyl, C₀₋₆alkylaryl and C₀₋₆alkylheteroaryl;
- 20 R⁸ and R⁹ may together form a 5 or 6 membered heterocyclic ring containing one or more heteroatoms selected from N, O or S, which heterocyclic ring may be optionally substituted by A;
R¹⁰ is hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₀₋₆alkylC₃₋₆cycloalkyl, C₀₋₆alkylaryl, C₀₋₆alkylheteroaryl or C₁₋₆alkylNR⁸R⁹;
- 25 R¹¹ is C₁₋₆alkylNR⁸R⁹;
R¹⁰ and R¹¹ may together form a 5 or 6 membered heterocyclic ring containing one or more heteroatoms selected from N, O or S, which heterocyclic ring may be optionally substituted by A;
- 30 R¹² is a 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A; wherein any C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₀₋₆alkylC₃₋₆cycloalkyl,

C₀₋₆alkylheterocycloalkyl, C₀₋₆alkylaryl, C₀₋₆alkylheteroaryl defined under R⁵ to R¹² may be substituted by one or more A;

A is halo, oxo (=O), nitro, CHO, CN, OR⁶, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₀₋₆alkylC₃₋₆cycloalkyl, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C₀₋₆alkylNR⁶R⁷, OC₁₋₆alkylNR⁶R⁷, CO₂R⁸, CONR⁶R⁷,
 5 NR⁶(CO)R⁶, O(CO)R⁶, COR⁶, SR⁶, (SO₂)NR⁶R⁷, (SO)NR⁶R⁷, SO₃R⁶, SO₂R⁶ or SOR⁶;

as a free base or a pharmaceutically acceptable salt, solvate or solvate of a salt thereof.

2. A compound according to claim 1, wherein Z and X is N; P is phenyl; R is

10 C₀₋₆alkyl(SO₂)NR¹R²; and m is 0.

3. A compound according to claim 2, wherein R¹ and R² in C₀₋₆alkyl(SO₂)NR¹R² together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms selected from N, O or S.

15

4. A compound according to claim 3, wherein said heterocyclic ring comprises one or more N heteroatoms and said heterocyclic ring is optionally substituted by A, preferably a C₁₋₆alkyl.

20 5. A compound according to any one of claims 1 to 4, wherein Y is CONR⁵; R⁵ is hydrogen; Q is C₁₋₆alkyl; R⁴ is selected from: phenyl, 5 or 6 membered heteroaromatic ring containing one or more heteroatoms independently selected from N, O, or S or a 5 or 6 membered heterocyclic ring containing one or two heteroatoms selected independently from N, O, or S which heterocyclic group may be saturated or unsaturated, CN, OR⁶,
 25 SO₂R⁶, NR⁶(CO)R⁷, (SO₂)NR⁶R⁷, and CONR⁶R⁷; and n is 1; said phenyl or 5 or 6 membered heterocyclic ring optionally substituted by A.

6. A compound according to claim 5, wherein A is selected from OR⁶, C₁₋₆alkyl, oxo (=O) and nitro; and R⁶ and/or R⁷ is selected from C₁₋₆alkyl and hydrogen.

7. A compound which is

3-Amino-*N*-(2-cyanoethyl)-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide;

3-Amino-*N*-(3-amino-3-oxopropyl)-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-

carboxamide;

3-Amino-*N*-(2-nitrobenzyl)-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide

3-Amino-*N*-(2-methoxybenzyl)-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide;

3-Amino-*N*-(3-morpholin-4-ylpropyl)-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-

carboxamide;

3-Amino-*N*-[3-(4-methylpiperazin-1-yl)propyl]-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide;

as a free base or a pharmaceutically acceptable salt, solvate or solvate of a salt thereof;

3-Amino-*N*-(2-morpholin-4-ylethyl)-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide hydrochloride;

3-Amino-*N*-[2-(1*H*-imidazol-4-yl)ethyl]-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide hydrochloride;

3-Amino-*N*-[3-(1*H*-imidazol-1-yl)propyl]-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide hydrochloride;

3-Amino-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}-*N*-(2-thien-2-ylethyl)pyrazine-2-carboxamide hydrochloride;

3-Amino-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}-*N*-(thien-2-ylmethyl)pyrazine-2-carboxamide hydrochloride;

3-Amino-*N*-(2-methoxyethyl)-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}pyrazine-2-carboxamide hydrochloride;

3-Amino-*N*-(3-methoxypropyl)-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}pyrazine-2-carboxamide hydrochloride;

3-Amino-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}-*N*-[3-(2-oxopyrrolidin-1-yl)propyl]pyrazine-2-carboxamide hydrochloride;

3-Amino-*N*-(cyanomethyl)-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}pyrazine-2-carboxamide dihydrochloride;

3-Amino-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-*N*-[2-(1*H*-pyrrol-1-yl)ethyl]-2-pyrazinecarboxamide hydrochloride;

3-Amino-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-*N*-[2-(methylsulfonyl)ethyl]-2-pyrazinecarboxamide hydrochloride;

5 *N*-[2-(Acetylamino)ethyl]-3-amino-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-2-pyrazinecarboxamide hydrochloride;

3-Amino-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-*N*-[2-(2-oxo-1-imidazolidinyl)ethyl]-2-pyrazinecarboxamide hydrochloride;

10 3-Amino-*N*-[2-(aminosulfonyl)ethyl]-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-2-pyrazinecarboxamide hydrochloride;

or as a free base or an alternative pharmaceutically acceptable salt, solvate or solvate of a salt thereof;

15 8. A pharmaceutical formulation comprising as active ingredient a therapeutically effective amount of the compound according to any one of claims 1 to 7 in association with pharmaceutically acceptable carriers or diluents.

9. The pharmaceutical formulation according to claim 8 for use in the prevention and/or treatment of conditions associated with glycogen synthase kinase-3.

20

10. A compound as defined in any one of claims 1 to 7 for use in therapy.

11. Use of a compound according to any one of claims 1 to 7 in the manufacture of a medicament for prevention and/or treatment of conditions associated with glycogen
25 synthase kinase-3.

12. Use of a compound according to any one of claims 1 to 7 in the manufacture of a medicament for prevention and/or treatment of dementia, Alzheimer's Disease, Parkinson's Disease, Frontotemporal dementia Parkinson's Type, Parkinson dementia
30 complex of Guam, HIV dementia, diseases with associated neurofibrillar tangle pathologies and dementia pugilistica.

13. The use according to claim 12 wherein the prevention and/or treatment is for Alzheimer's Disease.

14. Use of a compound according to any one of claims 1 to 7 in the manufacture of a
5 medicament for prevention and/or treatment of amyotrophic lateral sclerosis, corticobasal degeneration, Down syndrome, Huntington's Disease, postencephalatic parkinsonism, progressive supranuclear palsy, Pick's Disease, Niemann-Pick's Disease, stroke, head trauma and other chronic neurodegenerative diseases, Bipolar Disease, affective disorders, depression, schizophrenia, cognitive disorders, hair loss and contraceptive medication,
10 Type I and Type II diabetes, diabetic neuropathy and diabetes related disorders.

15. Use of a compound according to claim 14, wherein the prevention and/or treatment is Type I and Type II diabetes, diabetic neuropathy and diabetes related disorders.

16. Use of a compound according to any one of claims 1 to 7 in the manufacture of a
15 medicament for prevention and/or treatment of predemented states, Mild Cognitive Impairment, Age-Associated Memory Impairment, Age-Related Cognitive Decline, Cognitive Impairment No Dementia, mild cognitive decline, mild neurocognitive decline, Late-Life Forgetfulness, memory impairment and cognitive impairment, vascular
20 dementia, dementia with Lewy bodies, Frontotemporal dementia and androgenetic alopecia.

17. A method of prevention and/or treatment of conditions associated with glycogen synthase kinase-3, comprising administering to a mammal, including man in need of such
25 prevention and/or treatment, a therapeutically effective amount of a compound of formula I as defined in any one of claims 1 to 7.

18. A method of prevention and/or treatment of dementia, Alzheimer's Disease, Parkinson's Disease, Frontotemporal dementia Parkinson's Type, Parkinson dementia
30 complex of Guam, HIV dementia, diseases with associated neurofibrillar tangle pathologies and dementia pugilistica, comprising administering to a mammal, including

man in need of such prevention and/or treatment, a therapeutically effective amount of a compound of formula I as defined in any one of claims 1 to 7.

19. The method according to claim 18, wherein the prevention and/or treatment is for
5 Alzheimer's Disease.

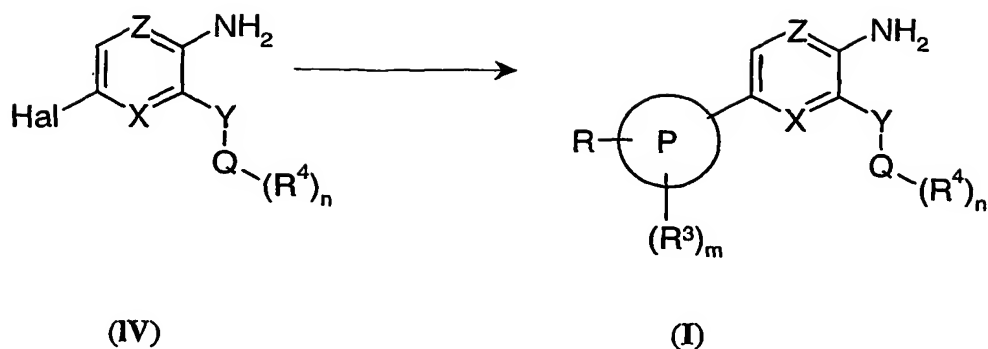
20. A method of prevention and/or treatment of amyotrophic lateral sclerosis, corticobasal degeneration, Down syndrome, Huntington's Disease, postencephalatic parkinsonism, progressive supranuclear palsy, Pick's Disease, Niemann-Pick's Disease, stroke, head
10 trauma and other chronic neurodegenerative diseases, Bipolar Disease, affective disorders, depression, schizophrenia, cognitive disorders, hair loss and contraceptive medication, Type I and Type II diabetes, diabetic neuropathy and diabetes related disorders, comprising administering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound of formula I as defined in any
15 one of claims 1 to 7.

21. The method according to claim 18, wherein the prevention and/or treatment is Type I and Type II diabetes, diabetic neuropathy and diabetes related disorders.

22. A method of prevention and/or treatment of predemented states, Mild Cognitive Impairment, Age-Associated Memory Impairment, Age-Related Cognitive Decline, Cognitive Impairment No Dementia, mild cognitive decline, mild neurocognitive decline, Late-Life Forgetfulness, memory impairment and cognitive impairment, vascular
20 dementia, dementia with Lewy bodies, Frontotemporal dementia and androgenetic alopecia, comprising administering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound of formula I as defined in any one of claims 1 to 7.

23. A process for the preparation of a compound of formula I according to claim 1,
30 wherein Y, X, Z, P, Q, R, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², A, m and n are defined as in formula I, comprising of de-halogen coupling of a compound of formula IV with an appropriate aryl species;

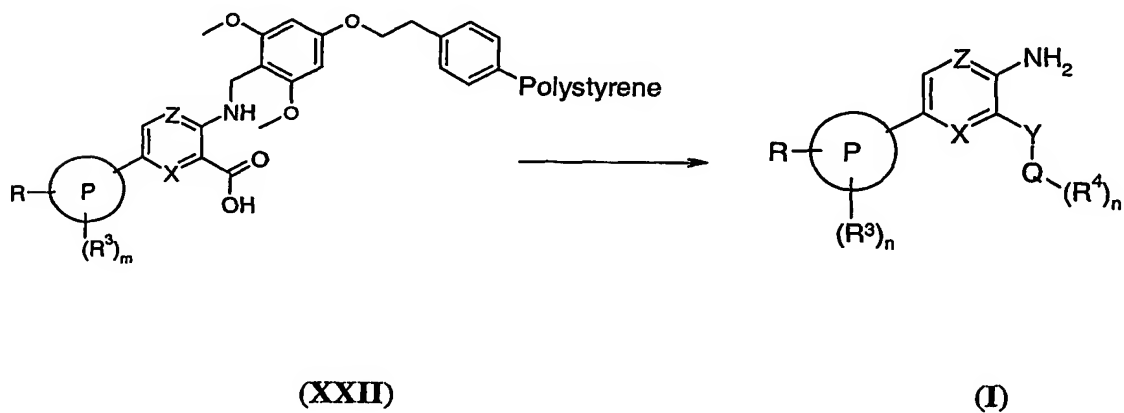
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5 to give a compound of formula I.

24. A process for the preparation of a compound of formula I according to claim 1, wherein Y, X, Z, P, Q, R, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², A, m and n are defined as in formula I, comprising reacting of a compound of formula XXII:

10

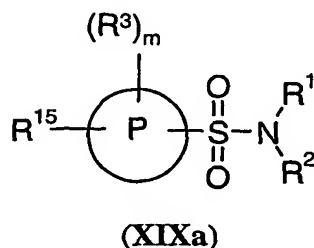


15

wherein the reaction is being performed by activation of a compound of formula XXII by treatment with a coupling agent or with an acyl halide reagent followed by treatment with the appropriate amine, followed by cleavage of the solid phase moiety by treatment with an suitable acid in a suitable solvent, and where the reaction temperature is between 0 °C and reflux, to give a compound of formula I.

20

25. A compound of formula **XIXa**



5 wherein

P is phenyl

R^1 and R^2 are independently selected from hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkyl C_{3-6} cycloalkyl, C_{0-6} alkylheterocycloalkyl, C_{1-6} alkyl NR^6R^7 ,

C_{0-6} alkylaryl and C_{0-6} alkylheteroaryl, wherein any C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl,

10 C_{0-6} alkyl C_{3-6} cycloalkyl, C_{0-6} alkylheterocycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheteroaryl may be substituted by one or more A;

R^1 and R^2 may together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

15 R^3 is independently selected from halogen, nitro, CHO, C_{0-6} alkylCN, OC_{1-6} alkylCN,

C_{0-6} alkylOR⁶, OC_{1-6} alkylOR⁶, fluoromethyl, difluoromethyl, trifluoromethyl,

fluoromethoxy, difluoromethoxy, trifluoromethoxy, C_{0-6} alkyl NR^6R^7 , OC_{1-6} alkyl NR^6R^7 ,

OC_{1-6} alkyl OC_{1-6} alkyl NR^6R^7 , NR^6OR^7 , C_{0-6} alkylCO₂R⁶, OC_{1-6} alkylCO₂R⁶,

C_{0-6} alkylCONR⁶R⁷, OC_{1-6} alkylCONR⁶R⁷, OC_{1-6} alkyl $NR^6(CO)R^7$, C_{0-6} alkyl $NR^6(CO)R^7$,

20 $O(CO)NR^6R^7$, $NR^6(CO)OR^7$, $NR^6(CO)NR^6R^7$, $O(CO)OR^6$, $O(CO)R^6$, C_{0-6} alkylCOR⁶,

OC_{1-6} alkylCOR⁶, $NR^6(CO)(CO)R^6$, $NR^6(CO)(CO)NR^6R^7$, SR^6 , C_{0-6} alkyl(SO₂) NR^6R^7 ,

OC_{1-6} alkyl $NR^6(SO_2)R^7$, OC_{0-6} alkyl(SO₂) NR^6R^7 , C_{0-6} alkyl(SO) NR^6R^7 ,

OC_{1-6} alkyl(SO) NR^6R^7 , SO_3R^6 , C_{0-6} alkyl $NR^6(SO_2)NR^6R^7$, C_{0-6} alkyl $NR^6(SO)R^7$,

OC_{1-6} alkyl $NR^6(SO)R^7$, OC_{0-6} alkylSO₂R⁶, C_{0-6} alkylSO₂R⁶, C_{0-6} alkylSOR⁶, C_{1-6} alkyl,

25 C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkyl C_{3-6} cycloalkyl, C_{0-6} alkylaryl and C_{0-6} alkylheteroaryl,

wherein any C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkyl C_{3-6} cycloalkyl, C_{0-6} alkylaryl and C_{0-6} alkylheteroaryl may be optionally substituted by one or more A;

R^6 and R^7 are independently selected from hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkyl C_{3-6} cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheteroaryl and C_{1-6} alkyl NR^8R^9 ;

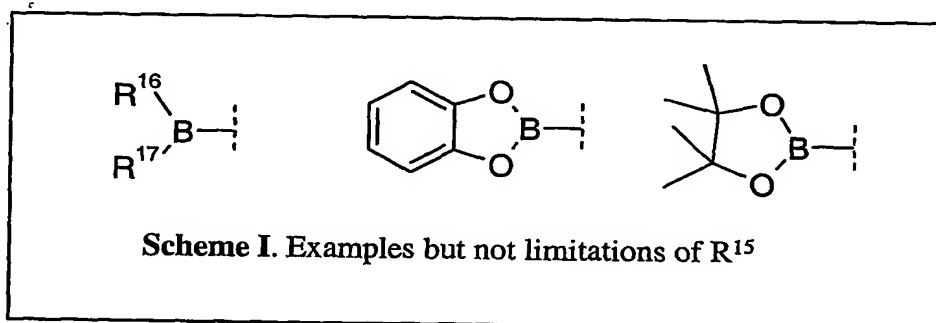
R^6 and R^7 may together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A and wherein a CH_2 group may optionally be replaced by a CO group;

- 5 R^8 and R^9 are independently selected from hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{0-6} alkyl C_{3-6} cycloalkyl, C_{0-6} alkylaryl and C_{0-6} alkylheteroaryl;

R^8 and R^9 may together form a 5 or 6 membered heterocyclic ring containing one or more heteroatoms selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

- 10 m is 0, 1, 2, 3 or 4;

R^{15} is a group outlined in Scheme I, wherein R^{16} and R^{17} are hydroxy and B is boron;



A is halogen, oxo ($=O$), nitro, CHO, CN, OR^6 , C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl,

- 15 C_{0-6} alkyl C_{3-6} cycloalkyl, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C_{0-6} alkyl NR^6R^7 , OC_{1-6} alkyl NR^6R^7 , CO_2R^8 , $CONR^6R^7$, $NR^6(CO)R^6$, $O(CO)R^6$, COR^6 , SR^6 , $(SO_2)NR^6R^7$, $(SO)NR^6R^7$, SO_3R^6 , SO_2R^6 or SOR^6 , as a free base or a salt, solvate or solvate of a salt thereof.

- 20 26. A compound according to claim 25, wherein

R^1 and R^2 together forms a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

m is 0;

- 25 A is C_{1-6} alkyl; as a free base or a salt, solvate or solvate of a salt thereof.

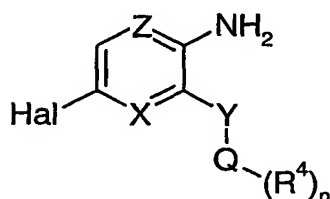
27. A compound which is

4-(Pyrrolidin-1-ylsulfonyl)phenylboronic acid;

4-[(4-Methylpiperazin-1-yl)sulfonyl]phenylboronic acid;

5 as a free base or a salt, solvate or solvate of a salt thereof.

28. A compound of formula IV



10 (IV)

wherein

Y is CONR^5 , NR^5CO , SO_2NR^5 , NR^5SO_2 , CH_2NR^5 , NR^5CONR^5 , CH_2CO , CO or CH_2O ;

X is CH or N;

Z is N;

15 Q is $\text{C}_{1-6}\text{alkyl}$, $\text{C}_{2-6}\text{alkenyl}$ or $\text{C}_{2-6}\text{alkynyl}$;

R^4 is independently selected from halogen, nitro, CHO, CN, $\text{OC}_{1-6}\text{alkylCN}$, OR^6 ,

$\text{OC}_{1-6}\text{alkylOR}^6$, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy,

difluoromethoxy, trifluoromethoxy, NR^6R^7 , $\text{OC}_{1-6}\text{alkylNR}^6\text{R}^7$, NR^6OR^7 , CO_2R^6 ,

$\text{OC}_{1-6}\text{alkylCO}_2\text{R}^6$, CONR^6R^7 , $\text{OC}_{1-6}\text{alkylCONR}^6\text{R}^7$, $\text{OC}_{1-6}\text{alkylNR}^6(\text{CO})\text{R}^7$, $\text{NR}^6(\text{CO})\text{R}^7$,

20 $\text{O}(\text{CO})\text{NR}^6\text{R}^7$, $\text{NR}^6(\text{CO})\text{OR}^7$, $\text{NR}^6(\text{CO})\text{NR}^6\text{R}^7$, $\text{O}(\text{CO})\text{OR}^6$, $\text{O}(\text{CO})\text{R}^6$, COR^6 ,

$\text{OC}_{1-6}\text{alkylCOR}^6$, $\text{NR}^6(\text{CO})(\text{CO})\text{R}^6$, $\text{NR}^6(\text{CO})(\text{CO})\text{NR}^6\text{R}^7$, SR^6 , $(\text{SO}_2)\text{NR}^6\text{R}^7$,

$\text{OC}_{1-6}\text{alkylNR}^6(\text{SO}_2)\text{R}^7$, $\text{OC}_{0-6}\text{alkyl}(\text{SO}_2)\text{NR}^6\text{R}^7$, $(\text{SO})\text{NR}^6\text{R}^7$, $\text{OC}_{1-6}\text{alkyl}(\text{SO})\text{NR}^6\text{R}^7$,

SO_3R^6 , $\text{NR}^6(\text{SO}_2)\text{NR}^6\text{R}^7$, $\text{NR}^6(\text{SO})\text{R}^7$, $\text{OC}_{1-6}\text{alkylNR}^6(\text{SO})\text{R}^7$, $\text{OC}_{0-6}\text{alkylSO}_2\text{R}^6$, SO_2R^6 ,

SOR^6 , $\text{C}_{3-6}\text{cycloalkyl}$, phenyl, a 5 or 6 membered heteroaromatic ring containing one or

25 more heteroatoms independently selected from N, O, or S, or a 5 or 6 membered

heterocyclic ring containing one or more heteroatoms independently selected from N, O, or

S which heterocyclic group may be saturated or unsaturated, and said phenyl ring or 5 or 6

membered heteroaromatic ring or 5 or 6 membered heterocyclic ring may optionally be

fused with a 5 or 6 membered saturated, partially saturated or unsaturated ring containing

atoms independently selected from C, N, O or S wherein any C₃₋₆cycloalkyl, phenyl, 5 or 6 membered heteroaromatic ring with one or two heteroatoms selected independently from N, O, or S or a 5 or 6 membered heterocyclic ring containing one or two heteroatoms selected independently from N, O, or S; may be optionally be substituted by one or more

5 A;

R⁵ is hydrogen or C₁₋₆alkyl

R⁶ and R⁷ are independently selected from hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₀₋₆alkylC₃₋₆cycloalkyl, C₀₋₆alkylaryl, C₀₋₆alkylheteroaryl and C₁₋₆alkylNR⁸R⁹;

R⁶ and R⁷ may together form a substituted 5 or 6 membered heterocyclic ring containing
10 one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A and wherein a CH₂ group may optionally be replaced by a CO group;

R⁸ and R⁹ are independently selected from hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₀₋₆alkylC₃₋₆cycloalkyl, C₀₋₆alkylaryl and C₀₋₆alkylheteroaryl;

15 R⁸ and R⁹ may together form a 5 or 6 membered heterocyclic ring containing one or more heteroatoms selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

Hal is halogen;

n is 0, 1, 2, 3 or 4;

20 A is halogen, oxo (=O), nitro, CHO, CN, OR⁶, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₀₋₆alkylC₃₋₆cycloalkyl, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C₀₋₆alkylNR⁶R⁷, OC₁₋₆alkylNR⁶R⁷, CO₂R⁸, CONR⁶R⁷, NR⁶(CO)R⁶, O(CO)R⁶, COR⁶, SR⁶, (SO₂)NR⁶R⁷, (SO)NR⁶R⁷, SO₃R⁶, SO₂R⁶ or SOR⁶; as a free base or a salt, solvate or solvate of a salt thereof.

25 29. A compound according to claim 28, wherein

Y is CONR⁵;

X is N;

Q is C₁₋₆alkyl;

30 R⁴ is independently selected from CN, OR⁶, a 5 or 6 membered heteroaromatic ring containing one or more heteroatoms independently selected from N, O, or S, or a 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected

from N, O, or S which heterocyclic group may be saturated or unsaturated, wherein any 5 or 6 membered heterocyclic ring containing one or two heteroatoms selected independently from N, O, or S; may be optionally be substituted by A;

R⁵ is hydrogen;

5 R⁶ is, C₁₋₆alkyl;

n is 1;

A is oxo (=O);

as a free base or a salt, solvate or solvate of a salt thereof.

10 30. A compound which is

3-Amino-6-bromo-*N*-(2-morpholin-4-ylethyl)pyrazine-2-carboxamide;

3-Amino-6-bromo-*N*-[2-(1*H*-imidazol-4-yl)ethyl]pyrazine-2-carboxamide;

3-Amino-6-bromo-*N*-[3-(1*H*-imidazol-1-yl)propyl]pyrazine-2-carboxamide;

3-Amino-6-bromo-*N*-(2-thien-2-ylethyl)pyrazine-2-carboxamide;

15 3-Amino-6-bromo-*N*-(thien-2-ylmethyl)pyrazine-2-carboxamide;

3-Amino-6-bromo-*N*-(2-methoxyethyl)pyrazine-2-carboxamide;

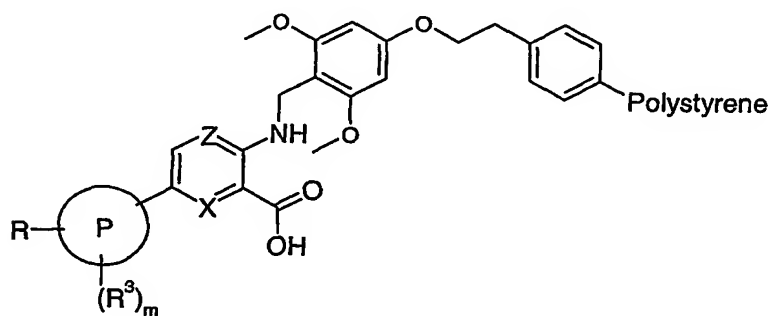
3-Amino-6-bromo-*N*-(3-methoxypropyl)pyrazine-2-carboxamide;

3-Amino-6-bromo-*N*-[3-(2-oxopyrrolidin-1-yl)propyl]pyrazine-2-carboxamide;

3-Amino-6-bromo-*N*-(cyanomethyl)pyrazine-2-carboxamide;

20 as a free base or a salt, solvate or solvate of a salt thereof.

31. A compound of formula **XXII**



(XXII)

wherein:

Z is N;

X is CH or N;

P is phenyl or a 5 or 6 membered heteroaromatic ring containing one or more heteroatoms
 5 selected from N, O or S and said phenyl ring or 5 or 6 membered heteroaromatic ring may optionally be fused with a 5 or 6 membered saturated, partially saturated or unsaturated ring containing atoms independently selected from C, N, O or S;

R is CHO, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C₀₋₆alkyl(SO₂)NR¹R²,
 OC₀₋₆alkyl(SO₂)NR¹R², OC₁₋₆alkyl(SO)NR¹R², C₁₋₆alkyl(SO)NR¹R², C₀₋₆alkylNR¹(SO)R²,
 10 OC₁₋₆alkylNR¹(SO)R², C₀₋₆alkylNR¹(SO₂)NR¹R², OC₁₋₆alkylNR¹(SO₂)R²,
 C₀₋₆alkyl(SO₂)C₁₋₆alkylNR¹R², OC₀₋₆alkyl(SO₂)C₁₋₆alkylNR¹R²,
 C₀₋₆alkyl(SO)C₁₋₆alkylNR¹R², OC₁₋₆alkyl(SO)C₁₋₆alkylNR¹R², C₀₋₆alkylSC₁₋₆alkylNR¹R²,
 OC₁₋₆alkylSC₁₋₆alkylNR¹R², OC₁₋₆alkylOC₁₋₆alkyl, C₁₋₆alkylOC₁₋₆alkylNR¹R²,
 OC₁₋₆alkylOC₁₋₆alkylNR¹R², C₀₋₆alkylCONR¹⁰R¹¹, OC₀₋₆alkylCONR¹R²,
 15 OC₁₋₆alkylNR¹R², C₀₋₆alkylNR¹⁰(CO)R¹¹, OC₁₋₆alkylNR¹(CO)R², C₀₋₆alkylNR¹¹(CO)R¹⁰,
 C₀₋₆alkylCOR¹¹, OC₁₋₆alkylCOR¹, C₀₋₆alkylNR¹⁰R¹¹, C₀₋₆alkylO(CO)R¹¹,
 OC₁₋₆alkylO(CO)R¹, C₀₋₆alkylC(NR¹⁰)NR¹⁰R¹¹, C₀₋₆alkylC(NR¹¹)N(R¹⁰)₂,
 OC₀₋₆alkylC(NR¹)NR¹R², C₀₋₆alkylNR¹⁰(CO)OR¹¹, OC₁₋₆alkylNR¹(CO)OR²,
 C₀₋₆alkylNR¹¹(CO)OR¹⁰, OC₁₋₆alkylCN, NR¹OR², C₀₋₆alkyl(CO)OR⁸, OC₁₋₆alkyl(CO)OR¹,
 20 NR¹(CO)NR¹R², NR¹(CO)(CO)R², NR¹(CO)(CO)NR¹R², OR¹² or SO₃R¹;

R¹ and R² are independently selected from hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl,
 C₀₋₆alkylC₃₋₆cycloalkyl, C₀₋₆alkylheterocycloalkyl, C₁₋₆alkylNR⁶R⁷,

C₀₋₆alkylaryl and C₀₋₆alkylheteroaryl, wherein any C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl,
 C₀₋₆alkylC₃₋₆cycloalkyl, C₀₋₆alkylheterocycloalkyl, C₀₋₆alkylaryl, C₀₋₆alkylheteroaryl may
 25 be substituted by one or more A;

R¹ and R² may together form a substituted 5 or 6 membered heterocyclic ring containing
 one or more heteroatoms independently selected from N, O or S, which heterocyclic ring
 may be optionally substituted by A;

R³ is independently selected from halogen, nitro, CHO, C₀₋₆alkylCN, OC₁₋₆alkylCN,

30 C₀₋₆alkylOR⁶, OC₁₋₆alkylOR⁶, fluoromethyl, difluoromethyl, trifluoromethyl,
 fluoromethoxy, difluoromethoxy, trifluoromethoxy, C₀₋₆alkylNR⁶R⁷, OC₁₋₆alkylNR⁶R⁷,
 OC₁₋₆alkylOC₁₋₆alkylNR⁶R⁷, NR⁶OR⁷, C₀₋₆alkylCO₂R⁶, OC₁₋₆alkylCO₂R⁶,

$C_{0-6}alkylCONR^6R^7$, $OC_{1-6}alkylCONR^6R^7$, $OC_{1-6}alkylNR^6(CO)R^7$, $C_{0-6}alkylNR^6(CO)R^7$,
 $O(CO)NR^6R^7$, $NR^6(CO)OR^7$, $NR^6(CO)NR^6R^7$, $O(CO)OR^6$, $O(CO)R^6$, $C_{0-6}alkylCOR^6$,
 $OC_{1-6}alkylCOR^6$, $NR^6(CO)(CO)R^6$, $NR^6(CO)(CO)NR^6R^7$, SR^6 , $C_{0-6}alkyl(SO_2)NR^6R^7$,
 $OC_{1-6}alkylNR^6(SO_2)R^7$, $OC_{0-6}alkyl(SO_2)NR^6R^7$, $C_{0-6}alkyl(SO)NR^6R^7$,
 $OC_{1-6}alkyl(SO)NR^6R^7$, SO_3R^6 , $C_{0-6}alkylNR^6(SO_2)NR^6R^7$, $C_{0-6}alkylNR^6(SO)R^7$,
 $OC_{1-6}alkylNR^6(SO)R^7$, $OC_{0-6}alkylSO_2R^6$, $C_{0-6}alkylSO_2R^6$, $C_{0-6}alkylSOR^6$, $C_{1-6}alkyl$,
 $C_{2-6}alkenyl$, $C_{2-6}alkynyl$, $C_{0-6}alkylC_{3-6}cycloalkyl$, $C_{0-6}alkylaryl$ and $C_{0-6}alkylheteroaryl$,
 wherein any $C_{1-6}alkyl$, $C_{2-6}alkenyl$, $C_{2-6}alkynyl$, $C_{0-6}alkylC_{3-6}cycloalkyl$, $C_{0-6}alkylaryl$ and
 $C_{0-6}alkylheteroaryl$ may be optionally substituted by one or more A;

R^6 and R^7 are independently selected from hydrogen, $C_{1-6}alkyl$, $C_{2-6}alkenyl$, $C_{2-6}alkynyl$,
 $C_{0-6}alkylC_{3-6}cycloalkyl$, $C_{0-6}alkylaryl$, $C_{0-6}alkylheteroaryl$ and $C_{1-6}alkylNR^8R^9$;

R^6 and R^7 may together form a substituted 5 or 6 membered heterocyclic ring containing
 one or more heteroatoms independently selected from N, O or S, which heterocyclic ring
 may be optionally substituted by A and wherein a CH_2 group may optionally be replaced
 by a CO group;

R^8 and R^9 are independently selected from hydrogen, $C_{1-6}alkyl$, $C_{2-6}alkenyl$, $C_{2-6}alkynyl$,
 $C_{0-6}alkylC_{3-6}cycloalkyl$, $C_{0-6}alkylaryl$ and $C_{0-6}alkylheteroaryl$;

R^8 and R^9 may together form a 5 or 6 membered heterocyclic ring containing one or more
 heteroatoms selected from N, O or S, which heterocyclic ring may be optionally

substituted by A;

R^{10} is hydrogen, $C_{1-6}alkyl$, $C_{2-6}alkenyl$, $C_{2-6}alkynyl$, $C_{0-6}alkylC_{3-6}cycloalkyl$,
 $C_{0-6}alkylaryl$, $C_{0-6}alkylheteroaryl$ or $C_{1-6}alkylNR^8R^9$;

R^{11} is $C_{1-6}alkylNR^8R^9$;

R^{10} and R^{11} may together form a 5 or 6 membered heterocyclic ring containing one or more
 heteroatoms selected from N, O or S, which heterocyclic ring may be optionally
 substituted by A;

A is halogen, oxo (=O), nitro, CHO, CN, OR^6 , $C_{1-6}alkyl$, $C_{2-6}alkenyl$, $C_{2-6}alkynyl$,
 $C_{0-6}alkylC_{3-6}cycloalkyl$, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy,
 difluoromethoxy, trifluoromethoxy, $C_{0-6}alkylNR^6R^7$, $OC_{1-6}alkylNR^6R^7$, CO_2R^8 , $CONR^6R^7$,
 $NR^6(CO)R^6$, $O(CO)R^6$, COR^6 , SR^6 , $(SO_2)NR^6R^7$, $(SO)NR^6R^7$, SO_3R^6 , SO_2R^6 or SOR^6 ;

m is 0, 1, 2, 3 or 4;

as a free base or a salt, solvate or solvate of a salt thereof.

32. A compound according to claim 31, wherein:

X is N;

P is phenyl;

5 R is C₀₋₆alkyl(SO₂)NR¹R²;

R¹ and R² may together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S;

m is 0;

as a free base or a salt, solvate or solvate of a salt thereof.

10

33. A compound which is

Methyl 3-{[2,6-dimethoxy-4-(2-phenylethoxy)benzyl]amino}-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxylate polystyrene;

3-{[2,6-Dimethoxy-4-(2-phenylethoxy)benzyl]amino}-6-[4-(pyrrolidin-1-

15 ylsulfonyl)phenyl]pyrazine-2-carboxylic acid polystyrene;

as a free base or a salt, solvate or solvate of a salt thereof.

34. The use of the intermediates according to any one of claims 25 to 33 for the preparation of a compound of formula I as defined in any one of claims 1 to 7.

20